ADRENOGENITAL SYNDROME

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ABSTRACT
The adrenogenital syndromes are inborn errors of metabolism that involve adrenal steroidogenesis and result in diverse hormonal, biochemical, and clinical effects. Recognition of these syndromes at birth in the child born with adrenogenital syndrome is crucial. In addition to facilitating assignment of sex of the child with ambiguous genitalia, recognition can be lifesaving, particularly in terms of prevention and treatment of electrolyte disorders. Several general statements are worthy of note regarding the adrenogenital syndromes.

Content of the article: The adrenogenital syndrome (AGS) is a relatively common inherited metabolic disease, generally caused by a deficiency of the adrenocortical enzyme steroid 21-hydroxylase. Incidence. Worldwide, the frequency of the classic form is estimated to be 1 in 5,000 to 15,000. However, in the Yupik indigenous people of Alaska, the disease occurs in up to 1 in 282 neonates. Genetic causes

Congenital adrenal hyperplasia mainly affects infants and is inherited as an autosomal recessive trait, meaning that it is not manifested unless the trait is inherited from both parents. The disorder is caused by any of several mutations in the genes encoding enzymes that are involved in the production of cortisol by the adrenal glands. The mutations vary from a single change in one of the nucleotide bases that constitute the gene to the deletion of the entire gene. The result of these mutations is a decrease in cortisol production. As a consequence, there is a compensatory increase in the secretion of an anterior pituitary hormone known as adrenocorticotropin. The high levels of adrenocorticotropin may restore cortisol secretion to near normal; however, they also stimulate the production of androgen and sometimes mineralocorticoids (hormones that stimulate retention of salt and water by the kidneys) by the adrenal cortex. The exact pattern and clinical manifestations of the disorder depend on the particular enzyme deficiency.

Types and clinical manifestation

The most common type of congenital adrenal hyperplasia is deficiency of 21-hydroxylase, an enzyme that catalyzes the next-to-last step in the synthesis of cortisol. In infants with partial 21-hydroxylase deficiency, the production of cortisol is near normal, but there is excess production of adrenal androgens. Excess androgen produced to overcome this deficiency

during fetal life results in virilization—the development of masculine-appearing external genitalia in newborn girls and precocious sexual development in boys—that becomes prominent as the child grows. There may also be decreased production of aldosterone, which leads to increased urinary excretion of sodium and water and decreased urinary excretion of potassium, resulting in low blood pressure, low serum sodium concentrations (hyponatremia), and high serum potassium concentrations (hyperkalemia). Severe 21-hydroxylase deficiency becomes evident soon after birth and may be fatal if not recognized and treated promptly.

The clinical manifestations of excess androgen production in utero that affect newborn genetic females include an enlarged clitoris, which may be mistaken for a penis; an enlarged vulva, which resembles a bilobed scrotum; and partial or complete fusion of the labia majora, with the opening of the urethra at the base of the clitoris. If not diagnosed early in life, girls with severe congenital adrenal hyperplasia, known as female pseudohermaphrodites, may be raised as boys and live thereafter as short, muscular men. These individuals are infertile and have only vestigial ovaries. There has been much debate as to whether genetic females who have been raised as boys can, when diagnosed late in childhood or in adolescence, assume the sexual identity of women. It appears that at least in some instances this is possible. Affected genetic males are more normal in appearance but may have penile enlargement. Continued excess androgen production in both girls and boys leads to rapid growth in the first years of life. However, the androgens also stimulate maturation and closure of the epiphyseal centres of bones so that linear growth ceases well before the usual age of puberty.

The frequency of 21-hydroxylase deficiency varies widely in different regions of the world, from as high as 1 in 300 births to lower than 1 in 20,000 births. Because the postnatal consequences are so severe, 21-hydroxylase deficiency is sometimes tested for as part of newborn screening programs.

Other, rarer forms of congenital adrenal hyperplasia result in varying degrees of hypertension or lack of sexual development, depending on the particular enzyme that is defective. Deficiency of 11-hydroxylase, an enzyme that catalyzes the last step in the synthesis of cortisol, leads to virilization and hypertension, the latter of which is caused by excess production of deoxycorticosterone, a mineralocorticoid similar to aldosterone. Deficiency of 17-hydroxylase leads to deficiency of estrogens and androgens and to excess deoxycorticosterone, causing sexual infantilism and hypertension. Congenital lipoid adrenal hyperplasia is caused by a defect in a very early step in the steroid synthetic pathway that results in glucocorticoid and mineralocorticoid deficiency and failure of development of secondary sex characteristics. Another genetic defect, 18-hydroxylase deficiency, results in aldosterone deficiency.

Diagnosis of CAH in children and young adults includes:

- Physical exam**.** Your health care provider will do a physical exam, check your child's blood pressure and heart rate, and review symptoms to identify possible CAH. The next step is to confirm the diagnosis with blood and urine tests.
- Blood and urine tests**.** These tests look for hormones produced by the adrenal glands at levels outside the standard ranges. The tests also check the levels of electrolytes. These are minerals such as sodium that balance the amount of water in the body.

- Genetic testing**.** Genetic testing may be needed to diagnose CAH.

Conclusion: This case may contribute to better understanding of the phenotype resulting from homozygote mutation R356W and heterozygote V281L in CYP21A2 gene, characterized by slight virilizing form of non-classic CAH. Our case suggests that gene sequencing must be done, as early as possible, in any small patient that have clinical and hormonal evidence of 21-hydroxylase deficiency. Actualy, CAH-associated clinical manifestation can be affected by the existence of a genetic variant.

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